* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

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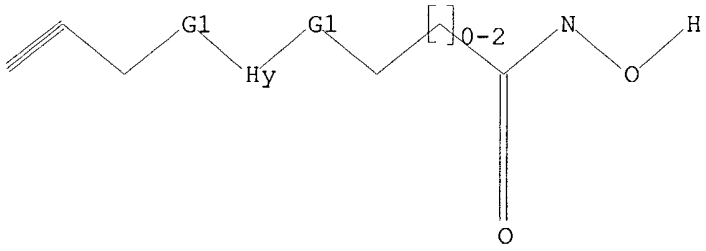

G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

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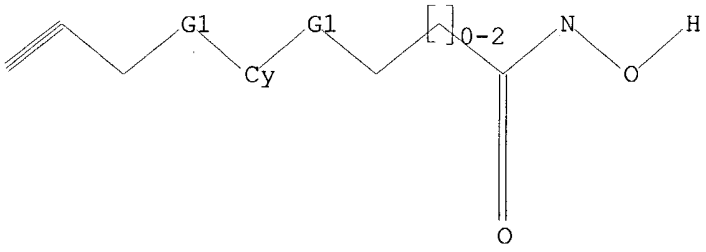


G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l4 full
L6 135 SEA SSS FUL L4

=> file ca

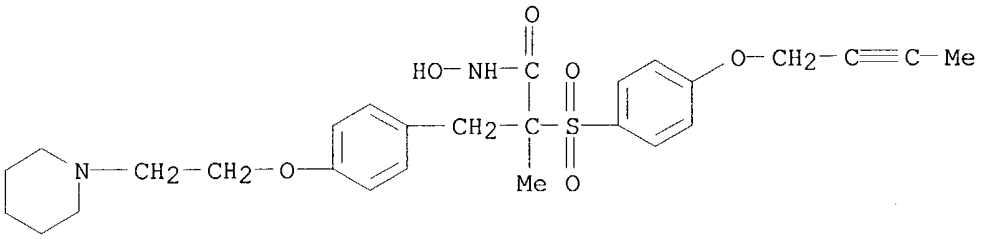
=> s l6
L7 3 L6

=> d ibib abs fhitstr 1-3

L7 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 136:118280 CA
TITLE: Preparation of N-hydroxy[(alkynyloxy)phenylsulfanyl]alkanoamides and analogs as TACE and MMP inhibitors
INVENTOR(S): Levin, Jeremy I.; Venkatesan, Aranapakam M.; Cole, Derek C.; Chen, James M.; Davis, Jamie M.; Grosu, George T.
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: U.S., 43 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6340691	B1	20020122	US 2000-492977	20000127
US 2002147342	A1	20021010	US 2001-55502	20011113

PRIORITY APPLN. INFO.: US 1999-160085P P 19990127
US 2000-492977 A3 20000127
OTHER SOURCE(S): MARPAT 136:118280
AB R1C.tplbond.CCR2R3Z1Z2Z3CR8R9ZCON(OH)R12 [I; R1 = H, alkyl, (hetero)aryl, etc.; R2,R3 = H, cyano, alkyl, CCH (sic); R8,R9 = H, aryl(alkyl), heteroaryl, etc.; R12 = H, heterocyclyl, (hetero)aryl, etc.; Z = bond, (un)substituted CH2, -CH2CH2; Z1 = O, SO0-2, (un)substituted NH, C (sic); Z2 = (hetero)arylene; Z3 = O, SO0-2, (un)substituted NH, CH (sic)] were prepd. Thus, MeCHBrCO2Et was thioetherified by 4-(HO)C6H4SH and the product etherified by MeC.tplbond.CCH2Br to give, in 2 addnl. steps, 4-(MeC.tplbond.CCH2O)C6H4SCHMeCONHOH. Data for biol. activity of I were given.
IT **287391-43-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-hydroxy[(alkynyloxy)phenylsulfanyl]alkanoamides and analogs as TACE and MMP inhibitors)
RN 287391-43-9 CA
CN Benzenepropanamide, .alpha.-[[4-(2-butynyloxy)phenyl]sulfonyl]-N-hydroxy-.alpha.-methyl-4-[2-(1-piperidinyl)ethoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 135:318704 CA
TITLE: Preparation of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivatives as selective matrix metalloproteinase inhibitors
INVENTOR(S): Park, Young-Jun; Bae, Hae-Young; Yoo, Ji-Uk; Chae, Myeong-Yun; Paek, Sang-Hyun; Min, Hye-Kyung; Park, Hyun-Gyu; Ryu, Choon-Ho; Kim, Kyung-Chul; Lee, Jeoung-Wook
PATENT ASSIGNEE(S): Samsung Electronics Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077092	A1	20011018	WO 2001-KR585	20010407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001048884	A5	20011023	AU 2001-48884	20010407
EP 1208092	A1	20020529	EP 2001-922101	20010407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530389	T2	20031014	JP 2001-575566	20010407
US 2002169314	A1	20021114	US 2001-18507	20011206
US 6548667	B2	20030415		

PRIORITY APPLN. INFO.:
KR 2000-18327 A 20000407
KR 2000-18328 A 20000407
KR 2000-18431 A 20000408
WO 2001-KR585 W 20010407

OTHER SOURCE(S): MARPAT 135:318704

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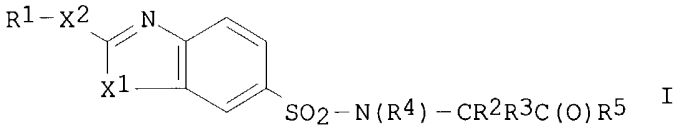

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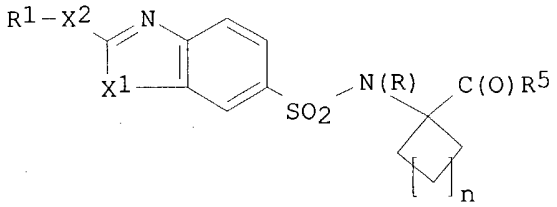

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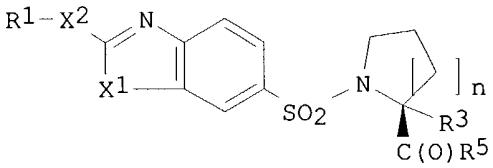

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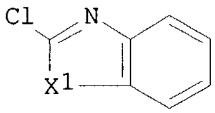


IV

AB The present invention provides novel sulfonamide derivs. (I (e.g. (2R)-3-methyl-2-[(2-phenylthiobenzothiazole-6-sulfonyl)amino]butanoic acid Me ester), II (n = 0-4) and III (n = 0-4)), useful as an inhibitors of matrix metalloproteinase (MMP), its isomers, pharmaceutically acceptable salts thereof and a process for prepg. the same. Since the sulfonamide derivs. of the present invention selectively inhibit MMP activity in vitro, the MMP inhibitors comprising the sulfonamide derivs. as an effective ingredient can be practically applied for the prevention and treatment of all sorts of diseases caused by overexpression and overactivation of MMP. In I: R1 denotes H, C1-12 alkyl, carbocyclic aryl-lower alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, C2-12 lower alkenyl, C2-12 lower alkynyl, carbocyclic aryl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, halo lower alkyl, biaryl-lower alkylarylalkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl-lower alkylpiperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R2 denotes H, lower alkyl, carbocyclic aryl-lower alkyl, C1-4 carbocyclic aryl-lower alkyl, C1-4 heterocyclic aryl-lower alkyl, C1-5 alkoxyphenyl-lower alkyl, C1-5 alkenoxyphenyl-lower alkyl, C1-5 alkynoxyphenyl-lower alkyl, heterocyclic aryl-lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, thio-lower alkyl, alkyl or aryl-(thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, carboxy-lower alkyl, (amino, mono or dialkylamino) lower alkyl or acylamino lower alkyl. R3 denotes H or C1-6-lower alkyl. R4 denotes H, C1-12 alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, carbocyclic aryl, carbocyclic aryl-lower alkyl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, biaryl-lower alkyl, halo lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl-(thio, sulfinyl or

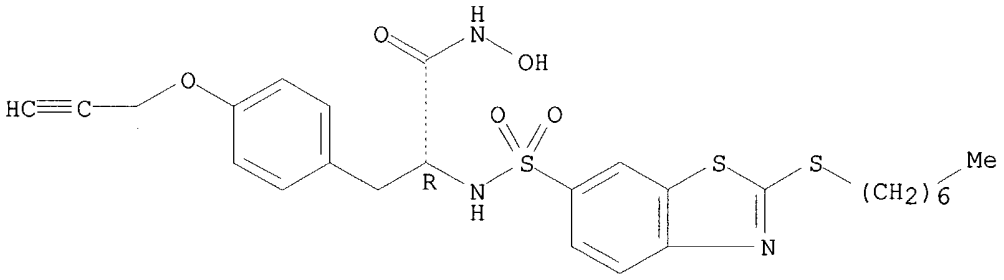
sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, carboxy lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl piperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R5 denotes hydroxy, alkoxy, halogen, thiol, thioalkoxy or hydroxylamine. X1 and X2 denote N-R7 (R7 is H, C1-6-lower alkyl, aryl, heteroaryl or arylalkyl), S or O. I can be prepd. by (i) reacting a sulfonyl halide with H2NCR2R3CO2R6 (R6 = protecting group) in an org. solvent in the presence of a base to give a sulfonamide; (ii) replacing the H on N using R4-L (L = reactive leaving group) in an org. solvent in the presence of a base; and (iii) hydrolyzing the intermediate to give I (R5 = OH), or further condensing I (R5 = OH) to prep. I (R5 = NHOH). Alternatively, I can be prepd. by (i) chlorosulfonylating IV; (ii) reacting this intermediate with an amino acid deriv. in an org. solvent in the presence of base to give a sulfonamide; (iii) heating this intermediate and R1-X2H together at 70 to 80.degree. in an org. solvent in the presence of base to cause substitution for Cl; (iv) reacting this intermediate with R4-L (L = reactive leaving group) in an org. solvent in the presence of base to cause substitution for H on N; and, (v) hydrolyzing this intermediate into I (R5 = OH), or further condensing I (R5= OH) to prep. I (R5 = NHOH). .apprx.70 Example prepns. of intermediates and products are given. Inhibition rates for some of the claimed compds. are reported for gelatinase A (MMP-2), gelatinase B (MMP-9) and collagenase (MMP-1).

IT **367517-41-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivs. as selective matrix metalloproteinase inhibitors)

RN 367517-41-7 CA

CN Benzenepropanamide, .alpha.-[[[2-(heptylthio)-6-benzothiazolyl]sulfonyl]amino]-N-hydroxy-4-(2-propynyloxy)-, (.alpha.R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 133:150348 CA
TITLE: Preparation of alkynyl containing hydroxamic acid compounds as TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Venkatesan, Aranapakam Mudumbai; Cole, Derek Cecil; Chen, James Ming; Davis, Jamie Marie; Grosu, George Theodore
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044713	A1	20000803	WO 2000-US2078	20000127
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356346	AA	20000803	CA 2000-2356346	20000127
EP 1147080	A1	20011024	EP 2000-911652	20000127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000007783	A	20020205	BR 2000-7783	20000127
AU 767754	B2	20031120	AU 2000-33515	20000127
ZA 2001005066	A	20020920	ZA 2001-5066	20010620
NO 2001003677	A	20010920	NO 2001-3677	20010726

PRIORITY APPLN. INFO.: US 1999-239088 A 19990127
WO 2000-US2078 W 20000127

OTHER SOURCE(S): MARPAT 133:150348
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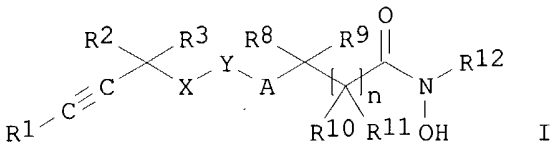

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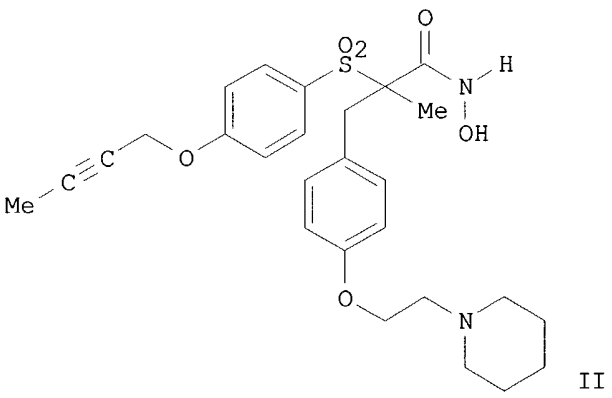


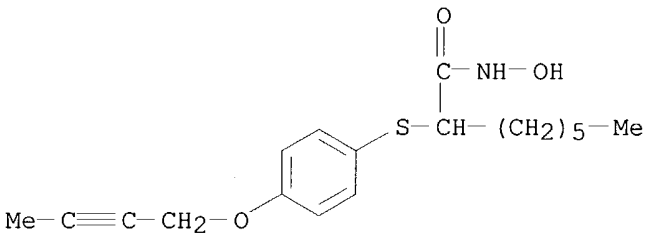
II

AB The title compds. [I; R1 = H, aryl, heteroaryl, etc.; R2, R3 = H, alkyl, CN, CCH; R8-R11 = H, aryl, aralkyl, etc.; R12 = H, aryl, 5-10 membered heteroaryl having 1-3 heteroatoms selected from N, S, O, etc.; A = O, S, SO, etc.; X = O, S, SO, etc.; Y = aryl, heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; n = 0-2] and their pharmaceutically acceptable salts, useful in treating disease conditions mediated by TNF-.alpha., such as rheumatoid arthritis, osteoarthritis, sepsis, AIDS, ulcerative colitis, multiple sclerosis, Crohn's disease and degenerative cartilage loss, were prepd. E.g., a multi-step synthesis of II.HCl which showed IC50 of 191 nM against TACE, and IC50 of 2 nM, 180 nM, and 200 nM against MMP-1, MMP-9, and MMP-13, resp., was given.

IT **287391-48-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of alkynyl contg. hydroxamic acid compds. as TACE inhibitors)

RN 287391-48-4 CA

CN Octanamide, 2-[[4-(2-butynyloxy)phenyl]thio]-N-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4               STRUCTURE UPLOADED
L5             5 S L4 SAM
L6           135 S L4 FULL

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L7             3 S L6

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10/055,502

Seaman, Margaret

Subject: FW: 502

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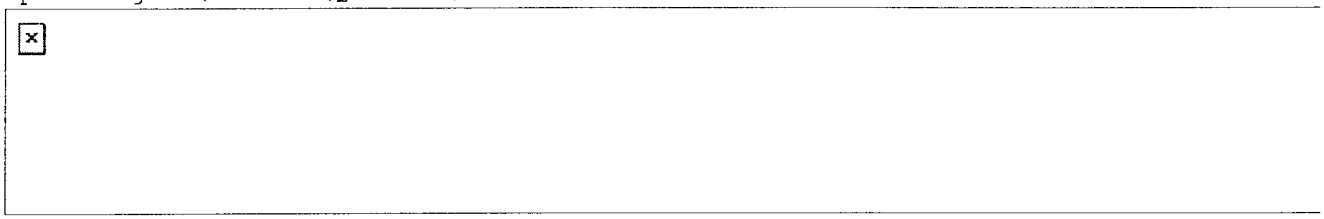

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exact/norm bonds :
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exact bonds :
4-5  5-8  14-15  15-16


G1:C,O,S,N

Match level :
1:Atom  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:CLASS  9:CLASS  12:CLASS
14:CLASS  15:CLASS  16:CLASS
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L1              STR
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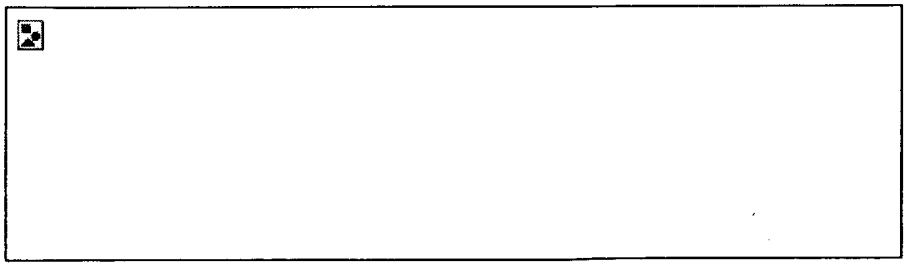

Structure attributes must be viewed using STN Express query preparation.

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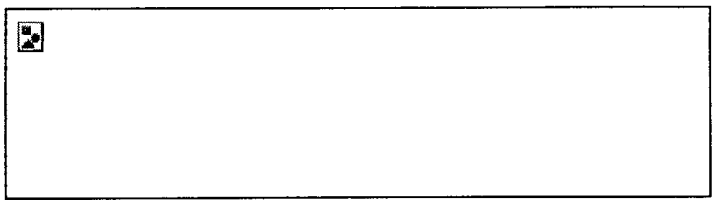
L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2004 ACS on STN
RN 287392-45-4 REGISTRY
CN Benzeneacetamide, α-[[4-(2-butynyloxy)phenyl]sulfinyl]-4-ethoxy-N-hydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H21 N O5 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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(PD<19990200)
L5 0 L4 AND PD<FEB 1999

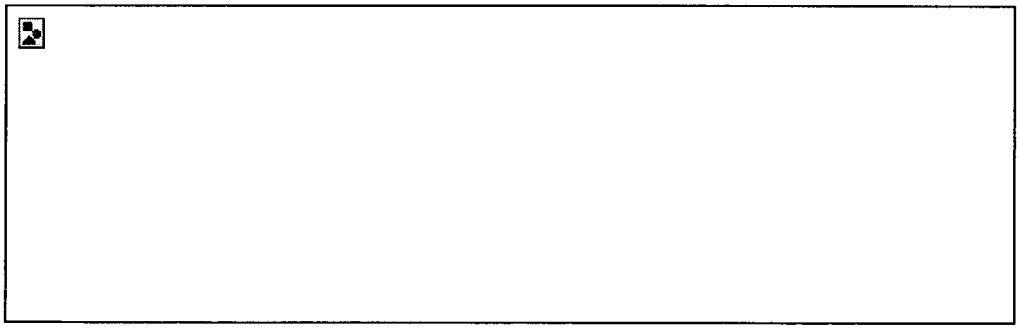
=> dis l4 1-3 bib abs fhitstr

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:66852 CAPLUS Full-text
DN 136:118280
TI Preparation of N-hydroxy[(alkynyloxy)phenylsulfanyl]alkanoamides and analogs as TACE and MMP inhibitors
IN Levin, Jeremy I.; Venkatesan, Aranapakam M.; Cole, Derek C.; Chen, James M.; Davis, Jamie M.; Grosu, George T.
PA American Cyanamid Company, USA
SO U.S., 43 pp.

CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6340691	B1	20020122	US 2000-492977	20000127
	US 2002147342	A1	20021010	US 2001-55502	20011113
PRAI	US 1999-160085P	P	19990127		
	US 2000-492977	A3	20000127		

OS MARPAT 136:118280
AB R1C.tplbond.CCR2R3Z1Z2Z3CR8R9ZCON(OH)R12 [I; R1 = H, alkyl, (hetero)aryl, etc.; R2,R3 = H, cyano, alkyl, CCH (sic); R8,R9 = H, aryl(alkyl), heteroaryl, etc.; R12 = H, heterocyclyl, (hetero)aryl, etc.; Z = bond, (un)substituted CH2, -CH2CH2; Z1 = O, SO0-2, (un)substituted NH, C (sic); Z2 = (hetero) arylene; Z3 = O, SO0-2, (un)substituted NH, CH (sic)] were prepared Thus, MeCHBrCO2Et was thioetherified by 4-(HO)C6H4SH and the product etherified by MeC.tplbond.CCH2Br to give, in 2 addnl. steps, 4-(MeC.tplbond.CCH2O) C6H4SCHMeCONHOH. Data for biol. activity of I were given.
IT **287391-43-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-hydroxy[(alkynyloxy)phenylsulfanyl]alkanoamides and analogs as TACE and MMP inhibitors)
RN 287391-43-9 CAPLUS
CN Benzenepropanamide, α-[[4-(2-butynyloxy)phenyl]sulfonyl]-N-hydroxy-α-methyl-4-[2-(1-piperidinyl)ethoxy]-, monohydrochloride (9CI) (CA INDEX NAME)



RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:762982 CAPLUS Full-text
DN 135:318704
TI Preparation of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivatives as selective matrix metalloproteinase inhibitors
IN Park, Young-Jun; Bae, Hae-Young; Yoo, Ji-Uk; Chae, Myeong-Yun; Paek, Sang-Hyun; Min, Hye-Kyung; Park, Hyun-Gyu; Ryu, Choon-Ho; Kim, Kyung-Chul; Lee, Jeoung-Wook
PA Samsung Electronics Co., Ltd., S. Korea
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077092	A1	20011018	WO 2001-KR585	20010407
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	AU 2001048884	A5	20011023	AU 2001-48884	20010407
	EP 1208092	A1	20020529	EP 2001-922101	20010407
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	JP 2003530389	T2	20031014	JP 2001-575566	20010407
	US 2002169314	A1	20021114	US 2001-18507	20011206
	US 6548667	B2	20030415		
PRAI	KR 2000-18327	A	20000407		
	KR 2000-18328	A	20000407		
	KR 2000-18431	A	20000408		
	WO 2001-KR585	W	20010407		

OS MARPAT 135:318704

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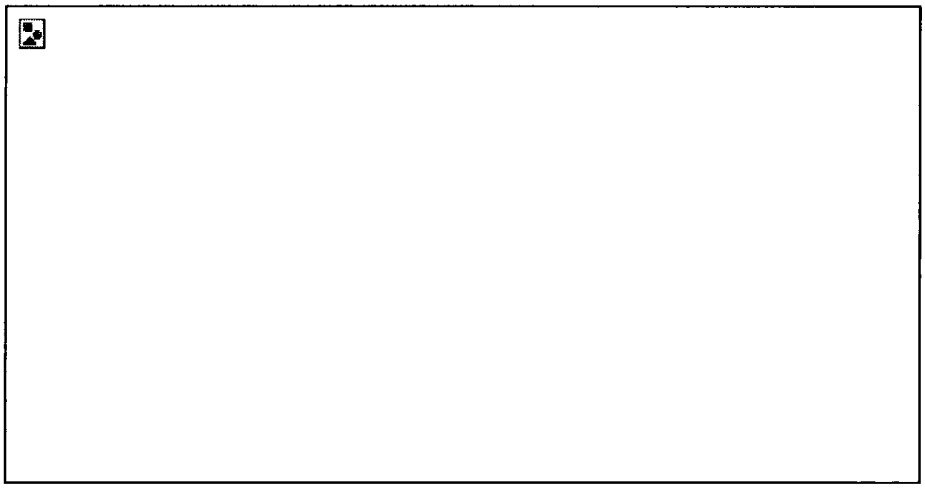


AB The present invention provides novel sulfonamide derivs. (I (e.g. (2R)-3-methyl-2-[(2-phenylthiobenzothiazole-6-sulfonyl)amino]butanoic acid Me ester), II (n = 0-4) and III (n = 0-4)), useful as an inhibitors of matrix metalloproteinase (MMP), its isomers, pharmaceutically acceptable salts thereof and a process for preparing the same. Since the sulfonamide derivs. of the present invention selectively inhibit MMP activity in vitro, the MMP inhibitors comprising the sulfonamide derivs. as an effective ingredient can be practically applied for the prevention and treatment of all sorts of diseases caused by overexpression and overactivation of MMP. In I: R1 denotes H, C1-12 alkyl, carbocyclic aryl-lower alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or

thio) C3-7 cycloalkyl-lower alkyl, C2-12 lower alkenyl, C2-12 lower alkynyl, carbocyclic aryl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, halo lower alkyl, biaryl-lower alkylarylalkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl (thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl-lower alkylpiperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R2 denotes H, lower alkyl, carbocyclic aryl-lower alkyl, C1-4 carbocyclic aryl-lower alkyl, C1-4 heterocyclic aryl-lower alkyl, C1-5 alkoxyphenyl-lower alkyl, C1-5 alkenoxyphenyl-lower alkyl, C1-5 alkynoxyphenyl-lower alkyl, heterocyclic aryl-lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, thio-lower alkyl, alkyl or aryl-(thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, carboxy-lower alkyl, (amino, mono or dialkylamino) lower alkyl or acylamino lower alkyl. R3 denotes H or C1-6-lower alkyl. R4 denotes H, C1-12 alkyl, C3-7 cycloalkyl, C3-7 cycloalkyl-lower alkyl, (oxo, amino or thio) C3-7 cycloalkyl, (oxo, amino or thio) C3-7 cycloalkyl-lower alkyl, carbocyclic aryl, carbocyclic aryl-lower alkyl, heterocyclic aryl, heterocyclic aryl-lower alkyl, biaryl, biaryl-lower alkyl, halo lower alkyl, hydroxy-lower alkyl, alkoxyalkyl, acyloxy-lower alkyl, alkyl or aryl-(thio, sulfinyl or sulfonyl) lower alkyl, (amino, mono or dialkylamino) lower alkyl, acylamino lower alkyl, carboxy lower alkyl, (N-lower alkylpiperazino, or N-carbocyclic or heterocyclic aryl piperazino)-lower alkyl or (morpholino, thiomorpholino, piperidino, pyrrolidino or piperidyl)-lower alkyl. R5 denotes hydroxy, alkoxy, halogen, thiol, thioalkoxy or hydroxylamine. X1 and X2 denote N-R7 (R7 is H, C1-6-lower alkyl, aryl, heteroaryl or arylalkyl), S or O. I can be prepared by (i) reacting a sulfonyl halide with H2NCR2R3CO2R6 (R6 = protecting group) in an organic solvent in the presence of a base to give a sulfonamide; (ii) replacing the H on N using R4-L (L = reactive leaving group) in an organic solvent in the presence of a base; and (iii) hydrolyzing the intermediate to give I (R5 = OH), or further condensing I (R5 = OH) to prepare I (R5 = NHOH). Alternatively, I can be prepared by (i) chlorosulfonylating IV; (ii) reacting this intermediate with an amino acid derivative in an organic solvent in the presence of base to give a sulfonamide; (iii) heating this intermediate and R1-X2H together at 70 to 80° in an organic solvent in the presence of base to cause substitution for Cl; (iv) reacting this intermediate with R4-L (L = reactive leaving group) in an organic solvent in the presence of base to cause substitution for H on N; and, (v) hydrolyzing this intermediate into I (R5 = OH), or further condensing I (R5= OH) to prepare I (R5 = NHOH). .apprx.70 Example prepns. of intermediates and products are given. Inhibition rates for some of the claimed compds. are reported for gelatinase A (MMP-2), gelatinase B (MMP-9) and collagenase (MMP-1).

IT **367517-41-7P**

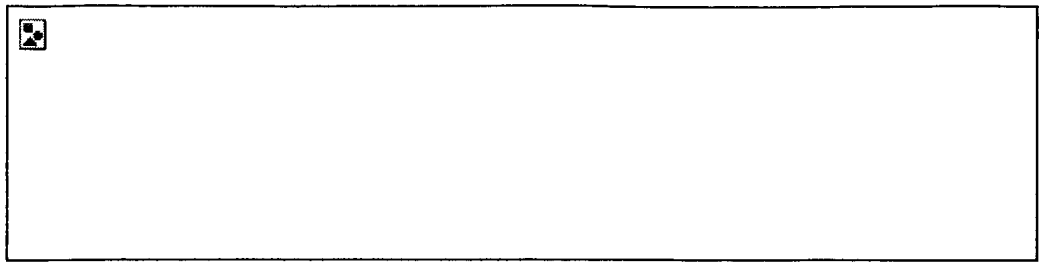
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of benzimidazole-, benzoxazole- and benzothiazolesulfonamide amino acid derivs. as selective matrix metalloproteinase inhibitors)

RN 367517-41-7 CAPLUS

CN Benzenepropanamide, α-[[[2-(heptylthio)-6-benzothiazolyl]sulfonyl]amino]-N-hydroxy-4-(2-propynyloxy)-, (αR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:535106 CAPLUS Full-text
DN 133:150348
TI Preparation of alkynyl containing hydroxamic acid compounds as TACE inhibitors
IN Levin, Jeremy Ian; Venkatesan, Aranapakam Mudumbai; Cole, Derek Cecil; Chen, James Ming; Davis, Jamie Marie; Grosu, George Theodore
PA American Cyanamid Company, USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044713	A1	20000803	WO 2000-US2078	20000127
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	CA 2356346	AA	20000803	CA 2000-2356346	20000127
	EP 1147080	A1	20011024	EP 2000-911652	20000127
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	BR 2000007783	A	20020205	BR 2000-7783	20000127
	AU 767754	B2	20031120	AU 2000-33515	20000127
	ZA 2001005066	A	20020920	ZA 2001-5066	20010620
	NO 2001003677	A	20010920	NO 2001-3677	20010726
PRAI	US 1999-239088	A	19990127		
	WO 2000-US2078	W	20000127		

OS MARPAT 133:150348
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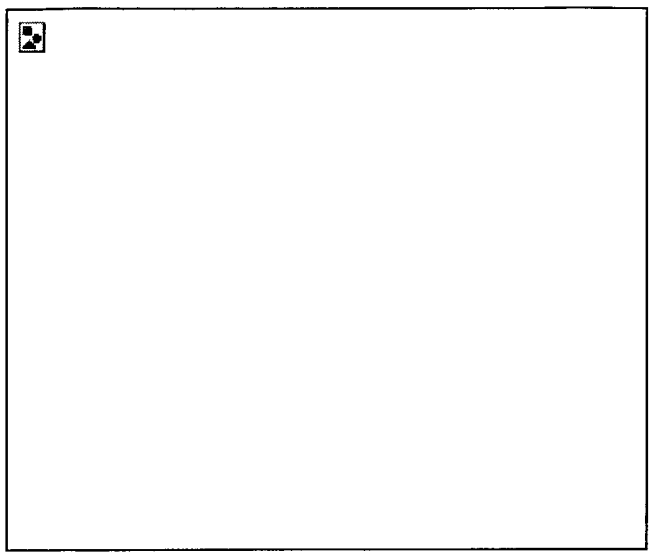
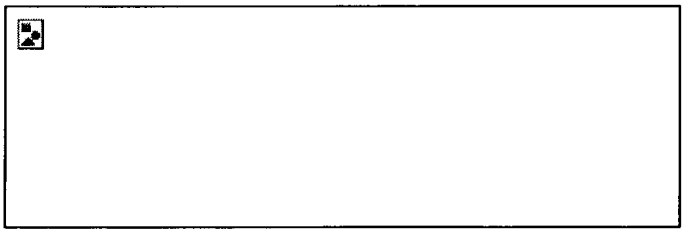


AB The title compds. [I; R1 = H, aryl, heteroaryl, etc.; R2, R3 = H, alkyl, CN, CCH; R8-R11 = H, aryl, aralkyl, etc.; R12 = H, aryl, 5-10 membered heteroaryl having 1-3 heteroatoms selected from N, S, O, etc.; A = O, S, SO, etc.; X = O, S, SO, etc.; Y = aryl, heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; n = 0-2] and their pharmaceutically acceptable salts, useful in treating disease conditions mediated by TNF-α, such as rheumatoid arthritis, osteoarthritis, sepsis, AIDS, ulcerative colitis, multiple sclerosis, Crohn's disease and degenerative cartilage loss, were prepared E.g., a multi-step synthesis of II.HCl which showed IC50 of 191 nM against TACE, and IC50 of 2 nM, 180 nM, and 200 nM against MMP-1, MMP-9, and MMP-13, resp., was given.

IT **287391-48-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alkynyl containing hydroxamic acid compds. as TACE inhibitors)

RN 287391-48-4 CAPLUS

CN Octanamide, 2-[[4-(2-butynyloxy)phenyl]thio]-N-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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